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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/962,094	10/31/97	BILLING-MEDEL	P 5995.US.P1

023492
ABBOTT LABORATORIES
DEPT. 377 - AP6D-2
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HM32/1205

EXAMINER	
ARTHUR,L	

ART UNIT	PAPER NUMBER
1655	21

DATE MAILED: 12/05/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/962,094	Billings-Medel et al.
Examiner	**Group Art Unit**
Lisa Athur	1655

[X] Responsive to communication(s) filed on *Aug 8, 2000*

[ ] This action is **FINAL.**

[ ] Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

[X] Claim(s) *1-13, 15-29, and 31-49* is/are pending in the applicat

Of the above, claim(s) *17-29, 31, 32, 34, 36, and 37* is/are withdrawn from consideration

[ ] Claim(s) _____ is/are allowed.

[X] Claim(s) *1-13, 15, 16, 33, 35, and 38-49* is/are rejected.

[ ] Claim(s) _____ is/are objected to.

[ ] Claims _____ are subject to restriction or election requirement.

Application Papers

[ ] See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

[ ] The drawing(s) filed on _____ is/are objected to by the Examiner.

[ ] The proposed drawing correction, filed on _____ is [ ] approved [ ] disapproved.

[ ] The specification is objected to by the Examiner.

[ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

[ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

[ ] All [ ] Some* [X] None of the CERTIFIED copies of the priority documents have been

[ ] received.

[ ] received in Application No. (Series Code/Serial Number) _____.

[ ] received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

[ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

[ ] Notice of References Cited, PTO-892

[ ] Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

[ ] Interview Summary, PTO-413

[ ] Notice of Draftsperson's Patent Drawing Review, PTO-948

[ ] Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. This application is a Continuing Prosecution Application filed August 8, 2000 under 37 CFR 1.53(d). Claims 1-13, 15,16, 33,35,38-49have been examined but claims 17-29,31,32,34,36,and 37 are withdrawn from consideration by the previously made restriction requirement. Any rejections made in the previous action which have been reiterated have been obviated by the amendments made to the claims. This action contains new grounds of rejection.

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

3. Claims 11-16,33,38,39 and newly added claims 43-48 are rejected under 35 U.S.C. 102(a) as being anticipated by Adams et al.(genbank accession no AA340069, from Nature 377(6547 Suppl.) 3-174 (1995)) and by Hillier et al. (Accession no. R75793, 1995)

Adams et al. Teach a 229 base pair expressed tag sequence (EST), i.e. a polynucleotide, which is about 90% identical to SEQ ID NO 1-5 of this application. (See attachment 1)

Hillier et al. Teach a 403 nucleotide EST containing clone which has 87.9%-95% sequence similarity with SEQ ID NO 1-5 of this application isolated from a human breast cDNA library (cells transfected with a vector containing the EST). (see attachment 1).

In light of the amendment of the claims the claims have an effective filing date of the parent application and now the cited references are art under 35 US.C. 102 (a) instead of 102(b).

MAINTAINED REJECTION

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-10,35,40-42 and 49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims have been amended to recite that the method is for detecting the presence of a polynucleotide indicative of breast disease by probing with a polynucleotide that specifically binds, encodes a mucin and has 90% identity with SEQ ID NO 1-4 and fragments or complements thereof and detecting the presence of the target polynucleotide and correlating the presence to the presence of breast disease. The specification teaches that SEQ ID Nos 1-3 are overlapping EST clones that were identified as being primarily representative of breast tissue libraries. SEQ ID NO 1-3 were used to make a contig which is SEQ ID NO 4 and SEQ. ID NO 5 represents the consensus sequence. SEQ ID NO 16 is the first forward frame translation of SEQ ID NO 5 which provides a 90 amino acids sequence. SEQ ID NO 4 was compared to the EST database and was found in 85.7 % of breast libraries and only 0.2% of non-breast libraries. The specification teaches that total RNA was obtained from solid breast tissue and from non-breast tissue and used for Northern blot analysis and RT-PCR . Figures 3A and 3B show the results of a

Northern blot analysis using SEQ ID NO 1 as a probe with RNA from normal breast tissue, normal prostate and cancer prostrate (3A) and from normal breast tissue and breast cancer tissue (3B). The probe hybridized with all normal breast 1/3 prostate cancer, 0 normal prostate, and 2/6 breast cancer. Table 1 showed than in 2/6 test breast cancer tissues there was over expression of the polynucleotide to which SEQ ID NO 1 hybridized. These data, however, do not support an association of expression of an mRNA to which SEQ ID NO 1 hybridizes with "breast disease". First, "diseases of the breast" is a broad term which is not limited to breast cancer but would encompass any type of disease of breast tissue, i.e. infections of breast tissue, mammary gland disorders, for example. The only breast disease tissue analyzed in the specification was breast cancer tissue. Second, the evidence in the specification does not predictably teach an association of a polynucleotide to which SEQ ID NO 1 hybridizes with breast cancer because the data is conflictory. In the northern blot analysis only two out of six breast cancer tissue samples showed expression of the polynucleotide complementary to SEQ ID NO 1. Four of the six breast cancer samples did not show expression of the polynucleotide as compared to five out of six normal breast tissue which did express the polynucleotide. From this assay, the skilled artisan would be lead to predict that the absence or decrease in expression of mRNA complementary to SEQ ID NO 1 might by associated with breast cancer as compared to normal breast tissue. However, the data in Table 1 seems to suggest that increased expression of an mRNA complementary to SEQ ID NO 1 was associated with breast cancer. Third, nowhere in the specification is there a teaching that SEQ ID NO s 1-4 encode a mucin. Consequently, since the

teachings in the specification are limited and do not allow the skilled artisan to drawn a reasonable and predictable conclusion as to an association with breast cancer, undue experimentation would be required of the skilled artisan to practice the claimed invention. Furthermore, the specification has not provided any guidance with regard to the presence of absence of a genomic DNA sequence which hybridizes with SEQ ID NO 1-5 and breast disease. The sequence appears to be present and expressed and normal breast tissue, but no conclusions can be made as to it's presence in the genome of other tissues because no teachings have been provided in the specification.

7. No claims are allowable over the prior art.

NEW GROUNDS OF REJECTION

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 1-13, 15,16, 33,35,38-49 are rejected under 35 U.S.C. 101 because the claimed invention lacks a specific and substantial asserted utility or a well-established utility.

The claims are drawn to a mthod ofr detecting breast disease in a patient by detecting the presence of a polynucleotide having 90% identity to SEQ ID NO 1-4 and which encodes a mucin

and correlating the presence of that polynucleotide to breast disease. This method lacks a ptentable utility because there is no specific or substantial use for this method. The specification has not disclosed a correlation between the recited plynucleotide and the existence of breast disease such that the skilled artisan would be able to have a real world context of use for the claimed method. The specification teaches that SEQ ID Nos 1-3 are overlapping EST clones that were identified as being primarily representative of breast tissue libraries. SEQ ID NO 1-3 were used to make a contig which is SEQ ID NO 4 and SEQ. ID NO 5 represents the consensus sequence. SEQ ID NO 16 is the first forward frame translation of SEQ ID NO 5 which provides a 90 amino acids sequence. SEQ ID NO 4 was compared to the EST database and was found in 85.7 % of breast libraries and only 0.2% of non-breast libraries. The specification teaches that total RNA was obtained from solid breast tissue and from non-breast tissue and used for Northern blot analysis and RT-PCR . Figures 3A and 3B show the results of a Northern blot analysis using SEQ ID NO 1 as a probe with RNA from normal breast tissue, normal prostate and cancer prostrate (3A) and from normal breast tissue and breast cancer tissue (3B). The probe hybridized with all normal breast 1/3 prostate cancer, 0 normal prostate, and 2/6 breast cancer. Table 1 showed than in 2/6 test breast cancer tissues there was over expression of the polynucleotide to which SEQ ID NO 1 hybridized. These data, however, do not support an association of expression of an mRNA to which SEQ ID NO 1 hybridizes with "breast disease". First, "diseases of the breast" is a broad term which is not limited to breast cancer but would encompass any type of disease of breast tissue, i.e. infections of breast tissue, mammary gland disorders, for example.

The only breast disease tissue analyzed in the specification was breast cancer tissue. Second, the evidence in the specification does not predictably teach an association of a polynucleotide to which SEQ ID NO 1 hybridizes with breast cancer because the data is conflictory. In the northern blot analysis only two out of six breast cancer tissue samples showed expression of the polynucleotide complementary to SEQ ID NO 1. Four of the six breast cancer samples did not show expression of the polynucleotide as compared to five out of six normal breast tissue which did express the polynucleotide. From this assay, the skilled artisan would be lead to predict that the absence or decrease in expression of mRNA complementary to SEQ ID NO 1 might by associated with breast cancer as compared to normal breast tissue. However, the data in Table 1 seems to suggest that increased expression of an mRNA complementary to SEQ ID NO 1 was associated with breast cancer. Third, nowhere in the specification is there a teaching that SEQ ID NO s 1-4 encode a mucin. Consequently, since the teachings in the specification are limited and do not allow the skilled artisan to drawn a reasonable and predictable conclusion as to an association with breast cancer, undue experimentation would be required of the skilled artisan to practice the claimed invention. Furthermore, the specification has not provided any guidance with regard to the presence of absence of a genomic DNA sequence which hybridizes with SEQ ID NO 1-4 and breast disease. The sequence appears to be present and expressed and normal breast tissue, but no conclusions can be made as to it's presence in the genome of other tissues because no teachings have been provided in the specification. Consequently, this alaysis shows that the claimed method had no real world context of use until a correlation can be established between

breast disease and the presence of the polynucleotides of SEQ ID NO 1-4. The showing the a particular seqeunce is overrepresented in a particular tissue is not considered a specific and substantial utility but is instead considered a general utility which a hiuge number of polynucleotides all possess.

8. Claims 1-13, 15,16, 33,35,38-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims as amended now recite that the polynucleotides encode a mucin. However, this amendment is not supported by the specification because no where in the specification is there a description of the polynucleotides of SEQ ID NO 1-5 encoding a mucin. The specification contains no teachings as to the protein which is may be encoded by the polynucleotides of the invention. The amendment appears to argue that the encoded protein and its function is inherent in the nucleotide sequence of SEQ ID nos 1-5. The evidence cited in the response, which is absent from the specification, is that the BS106 protein would be predicted to contain multiple sites for possible)-linked glycosylation. The response asserts that a BS106 protein bound to a peanut lectin, an orange lectin and a jacalin lectin which all recognize galactose but not to wheat germ lectin. The response asserts therefore that the BS106 protein has the same type of glycosylation as a mucin. These asserts which are not supported by evidence do not identify the BS106 protein as a mucin because many peoteins other than mucins are O-glycosylated. The

response also argues that BS106 is a mucin because it has a tandem repeating unit similar to mucins. However, again many proteins have such repeating units but are not mucins. Furthermore, as pointed out in the response the predicted molecular weights of BS106 and mucins are very different. Therefore, the asserts in the specification are not sufficient to establsih that the mucin functionality of the protein encoded by the BS106 polynucleotides is inherent in the sequence. Functionailtiy of the encoded protein woudl have to be established by expression of the BS106 described in the specification and a demonstration of that protein's function. Such evidence should be submitted in declaration form. However, because the specification contains no teaching that the polynucletoides of the claimed ivnention encode a mucin, this amendment introduces new matter into the application.

9. No claims are allowable.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa Arthur whose telephone number is (703) 308-3988. The examiner can normally be reached on Tuesday-Thursday from 7:00 AM to 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Primary Ex 1655

November 19, 2000